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decussation between the posterior halves of the medulla, on the one hand; and on the other, between each of these and the olivary body of the opposite side.

The memoir contains the details of other observations on the medulla of man and the lower animals.

XXVII. "On the Early Stages of Inflammation." By JOSEPH LISTER, Esq., F.R.C.S. Eng. and Edin., Assistant Surgeon to the Royal Infirmary of Edinburgh. Communicated by Dr. SHARPEY, Sec. R.S. Received June 18, 1857.

(Abstract.)

In this communication the author gives an account of an investigation with which he has been recently occupied, into the process of inflammation in the Frog's foot. The paper is divided into four sections, with an introduction and conclusion.

In the introduction it is observed, that "so far from our knowledge of inflammation being in a satisfactory condition, authorities are at variance upon the fundamental question whether it is to be regarded, in accordance with John Hunter's opinion, as active in its nature, and consisting in an exaltation of the functions of the affected part, or whether it should not rather be considered a passive result of diminished functional activity.....In seeking for the solution of this great problem, we cannot expect to gain much from the contemplation of the more advanced stages of inflammation.....It is upon the first deviations from health that the essential character of the morbid state will be most unequivocally stamped, and it is therefore to the early stages of inflammation that our attention must be chiefly directed."

Some cases are then mentioned to show that "in the early stages of inflammation in the human subject, whether induced by mechanical irritation or by an acrid application such as mustard, or of spontaneous origin, the minute vessels become abnormally loaded with red blood, the corpuscles of which ultimately become to a greater or less extent arrested prior to the occurrence of effusion." It is afterwards shown, from numerous facts, that "conclusions arrived at from the

study of the early stages of inflammation in the foot of the frog will apply in all strictness to the same morbid process in man."

The remainder of the introduction is occupied with a sketch of the principal theories which have been proposed to account for the obstruction to the progress of the blood-corpuscles in the early stages of inflammation.

The first section of the paper is devoted to the discussion of the aggregation of the corpuscles of the blood. It is shown by the author that the *rouleaux* "are simply the result of the disk-form of the corpuscles, together with a certain, though slight degree of adhesiveness which retains them pretty firmly attached together when in the position most favourable for its operation, namely when flat surface is applied to flat surface, but otherwise allows them to slip very readily upon one another." The aggregating tendency of the red disks is thus regarded as a phenomenon similar in kind, though inferior in degree, to the well-known adhesiveness of the white corpuscles. It is further shown, from numerous experiments, that the red corpuscles vary remarkably in adhesiveness, in consequence of changes in physical circumstances, or very slight chemical action.

Section II. is on the structure and functions of the blood-vessels.

Allusion is made to a paper by the author which will shortly appear in the Transactions of the Royal Society of Edinburgh, where he has recorded the observation, that in the smallest arteries of the web of the frog's foot the middle coat is composed of muscular fibre-cells wrapped spirally round the internal membrane. The parietes of the minute arteries are thus provided with a most efficient mechanism for diminution of calibre, and contrast in this respect very strikingly with the delicate nucleated membrane which constitutes the wall of a capillary. The functions of the two sets of vessels are described as being in harmony with these differences in structure; the arteries being specially characterized by contractility, while the capillaries exhibit only such changes of calibre as are explained by elasticity.

The thinness of the capillary wall is believed to favour the mutual interchanges between the blood and the tissues, but the consideration of some facts of physiology leads the author to the conclusion, that notwithstanding the distending force of the current of blood, the liquor sanguinis is not effused as a whole among the tissues in the state of health; and this is thought to imply that there subsists a

mutual repulsion between the materials of the capillary wall and the elements of the liquor sanguinis, preventing the passage of the latter into the pores of the former, except in so far as they are attracted by the tissues for the purposes of nutrition.

The heart is believed by the author to be the sole cause of the circulation of the blood in the frog's foot, and it is proved experimentally that other sources of movement cannot have more than a very trivial influence, and that their cessation, supposing them to exist at all, does not give rise to arrest of the blood or accumulation of corpuscles in the capillaries.

Distinct evidences of muscularity and contractility have been detected in the veins of the frog's foot, but compared with the arteries, the veins show very little spontaneous contraction.

Regarding the influence of changes in arterial calibre upon the blood in the capillaries, the author is led to conclude that "the arteries regulate by their contractility the amount of blood transmitted in a given time through the capillaries, but neither full dilatation, extreme constriction, nor any intermediate state of the former is capable *per se* of inducing accumulation of corpuscles in the latter."

The influence of the nervous system upon the arteries has formed the subject of a special experimental inquiry, the results of which are given in a supplement to the paper. It is there shown that the contractions of the arteries of the frog's web are regulated by a part of the spinal cord, the irritation of which induces complete constriction of the vessels, while its destruction is followed by permanent dilatation. Neither stimulation nor removal of the nervous centre for the arteries produces any perceptible change in the quality of the blood, as respects adhesiveness of its corpuscles or otherwise.

Section III., "on the effects of irritants upon the circulation in the frog's web," commences with an account of some experiments performed with tepid water applied for a brief period to the foot. This agent, which was selected as the mildest possible stimulant, produces in a very beautiful manner constriction of the arteries, followed by dilatation, with corresponding changes in the amount of blood transmitted through the capillaries, as explained at the close of Section II. When, however, such experiments were frequently repeated upon the same animal, and especially if the temperature of the water was more elevated, effects of a different kind began to show themselves; the

corpuscles of the blood experiencing obstruction to their progress even while the arteries were fully dilated, and the vessels consequently in the state most favourable, so far as their calibre was concerned, for transmitting the current of blood. If the irritation was still continued, the minute vessels became choked with closely packed corpuscles.

Subsequent experiments with a variety of other irritating agents showed that the corpuscles, both red and white, were obstructed in their progress through the irritated part, in consequence of their tending to adhere in an abnormal degree to one another and to the walls of the vessels. The effects upon the blood were always similar, although the means employed to produce irritation were exceedingly various, such as solutions of salts, mustard, essential oils, chloroform, heat, galvanic shock, mechanical violence, &c.

The irritant was generally so applied as to act only upon a small area of one of the webs, and it was found that the abnormal adhesiveness of the blood-corpuscles was in the first instance always precisely limited to the spot which had been thus acted on, though it frequently extended afterwards more or less to surrounding parts. At the same time the vessels of the irritated spot did not differ materially in calibre from those in its vicinity which participated in the arterial dilatation induced by the stimulus. The exact correspondence between the extent of the irritant application, and that of the effect upon the blood, showed that the latter must be due to direct action either upon the blood itself or the tissues of the web. That it was not the result of direct action upon the blood was evident from the two following considerations. In the first place, most of the agents employed to cause irritation, when applied to freshly drawn blood, either had no effect upon the corpuscles, or destroyed instead of increasing their adhesiveness. Secondly, if employed so as to act mildly on the web, they induced an abnormal condition of the blood, short of actual stagnation though very apparent, namely, slow movement of numerous and adhesive corpuscles; and this state of things might last, although the time of operation of the irritant was often limited to a few seconds, or even a still briefer period. Long after all the blood which could possibly have been directly acted on had left the vessels of the part, successive fresh portions continued to experience precisely

similar changes in passing through the irritated area. Hence the author considers the conclusion to be inevitable, "that the tissues, as distinguished from changes of calibre in the blood-vessels, are the primary seat of inflammation, and that the effects on the blood are secondary results of such derangement."

The remarkable fact discovered by Dr. H. Weber of Giessen, but observed independently by the author, that accumulation of corpuscles occurs in the vessels of a part irritated, after circulation has been arrested by a tight ligature round the thigh, furnished the opportunity for careful comparison between the conditions of blood in healthy and irritated parts uncomplicated by the effects of rapid movement. A series of experiments conducted in this way confirmed the conclusion previously arrived at, that the accumulation of the blood-corpuscles was simply the result of their abnormal adhesiveness. At the same time these experiments brought out the remarkable fact, that mere quiescence of the blood does not give rise to aggregation of the red corpuscles within the vessels, unless the tissues are in an unhealthy condition in consequence of irritation. It further appeared that the corpuscles never exhibit greater adhesiveness within the vessels of an inflamed part, than do those of blood from a healthy part when drawn from the body. Also, the well-known adhesiveness of the white corpuscles within the vessels does not occur, according to the author, unless some degree of irritation is present, and never exceeds that which is always seen in blood outside the body. Hence the inference is drawn, that the tissues of a healthy part exert an influence on the blood in their vicinity, by means of which the corpuscles, both red and white, are preserved free from adhesiveness; but that in an inflamed part this influence is more or less in abeyance.

This view has been confirmed by observations made on the wing of the Bat.

Also the comparison of drops of blood from healthy and inflamed parts in the human subject showed, that so soon as the blood was withdrawn from the vessels, the corpuscles of the former presented precisely the same degree of adhesiveness as those of the latter.

At the commencement of Section IV., "on the state of the tissues in inflammation," it is stated that "the conclusion arrived at in the latter part of the last section, that blood flowing through an

inflamed part behaves itself in the same way as when separated from the living body, naturally leads us to infer that the tissues of the inflamed part are in some degree approximated to the condition of dead matter, or, in other words, have suffered a diminution of power to discharge the offices peculiar to them as components of the healthy animal frame. This inference is strongly supported by considering what common effect is likely to be produced upon the tissues of the frog's web by all the various agents known to cause inflammatory disturbance of the circulation." It is then pointed out that all these agents, though differing greatly in their nature, agree in their tendency to inflict a lesion on the part to which they are applied, and impair the functional activity of the tissues. "But strong as are the arguments thus obtained by inference, it would be very desirable to confirm them by direct observation of the tissues. It fortunately happens that the pigmentary system of the frog is a tissue which, from its peculiar form and colour, is very apparent to the eye, so that it is easy to trace the remarkably active functions with which it is endowed, and their modifications under the influence of irritation."

The author then mentions the circumstances which led him to notice that the dark pigment of the frog presents remarkable differences of appearance at different times in one and the same animal; each dark patch being sometimes of stellate figure with minutely ramifying rays, at other times in the form of a small rounded spot. These changes had been before observed by some German writers, who attributed the rounded form to contraction of the branching rays of a stellate cell. This, however, the author finds to be erroneous, and in a supplementary section "on the anatomy and physiology of the pigmentary system of the frog," shows that the cells never change in form or size, but that the pigment-granules which are suspended in a colourless fluid are capable of being, on the one hand, attracted by a central force into a small space in the body of the cell, and, on the other hand, dispersed by a repulsive power into the minutest recesses of the ramifying rays. Both concentration and diffusion of the pigment may take place with great rapidity, implying remarkable energy in the attractive and repulsive forces, both of which appear to reside in a nucleus. The supplementary section concludes with some remarks on the physiological importance of the actual

observation of such attractions and repulsions in one of the animal tissues.

The paper continues with an account of an experimental investigation into the effects of irritants upon this function of the pigmentary system. Many experiments are related, all tending to support the general proposition, that "all agents, without any exception, which have the power of inducing accumulation of corpuscles and stagnation in the blood-vessels when applied to the web, paralyse at the same time the functions of the pigment-cells." It is also shown, from experiments upon amputated limbs free from blood, that this effect is independent of the state of the circulation. In cases of slight irritation, in which the blood resumes, after awhile, its natural characters (re-solution taking place), the paralysis of the pigment-cells is only temporary. "Thus the pigmentary system of the frog is a remarkably sensitive index of the condition of the affected tissue, and it is fortunate that its physical characters render it so easy to read its pointings. . . . The only other tissue of the frog's web, the functions of which can be observed by the eye, is that of the arterial muscular fibre-cells," and it is found that arteries passing through an inflamed area lose their power of contraction within the limits of that area, whereas the same vessels may be often seen to contract in other parts of their course.

"Thus, direct observation of the structures of the frog's web which discharge functions apparent to the eye, furnishes unequivocal support to the inference derived from other considerations, that in inflammation the tissues of the part, the primary seat of the affection, are in a state of diminished functional activity."

The "conclusion" consists of an inquiry how far the views expressed in the paper regarding the early stages of inflammation harmonize with the more advanced phenomena of the morbid process and with other facts of pathology.